relate to patentability, nor are they believed to introduce any new matter into the application.

The drawings have also been corrected in a similar manner, including the following changes to the drawings as shown in the attached relined copies thereof. More particularly, Fig. 1 has been changed to add "22" to the arrow between the leftmost compounder 16 and the compounding computer; also, the right compounder "16" has been changed to "15" to eliminate the duplication of reference numbers. In Fig. 4c, the number "14" has been changed to "144" and the number "140" has been added to the right of block 138. In Fig. 4d, the word "alter" has been changed to "alert" in block 164. "Block 160" has been changed to "block 162" and the horizontal line below line 158 has been omitted.

If the examiner approves of these drawing changes, they will be formally made and submitted in due course.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph beginning on page 10, line 25 has been changed as follows:

Broadly stated, the present invention is directed to a method and apparatus for controlling the compounding of pharmaceutical admixtures, where the compounding is done by one or more compounders that may be remotely located relative to the controller computer or admixtures, where the compounding is done by one or more compounders that may be remotely located relative to the controller computer or processing means that is interconnected with the compounders. Referring to FIG. 1, the controller computer or controller 10 has sufficient memory for storing pharmaceutical data in the form of a database as well as operating software for use in controlling compounders and other peripheral equipment. The computer 10 is preferably a multi-user, multi-tasking computer that has a communication interface for interconnecting to compounders 12, 14, 15 and 16 and other peripheral equipment such as printers 18 and 20 by communication links 22 that may be wired or wireless, may be part of a local area network, a wide area network or the Internet or a combination of the above. The computer 10 may have a display 23 and keyboard 25 as well as other accessories and features common to commercially available computers at this time.

The paragraph beginning on page 11, line 15 has been changed as follows:

Other peripheral equipment can include a dumb terminal 24 having a keyboard and display or other input device such as a laptop computer 26 or other handheld device that is adapted to enter prescriptions and input instructions for operating the controller computer software. The compounders may be located in different areas of a healthcare facility such as a hospital, or on different floors of a hospital or even at different hospitals. The compounders 12, [and] 14 and 15 as well as the printer 18 and terminal 24 are located in hospital B in FIG. 1, whereas the remainder of the equipment is shown to be located in hospital A. There is preferably a printer located near each compounder or combination of compounders, as shown, for printing labels that are applied to the prescribed admixtures that are compounded. The controller computer 10 is preferably interconnected with a general hospital computer 28 that may be used to prepare and record billing statements among other functions.

The paragraph beginning on page 12, line 3 has been changed as follows:

The present invention is adapted to control compounders such as compounders 12, 14, 15 and 16. The presence of [two] multiple machines in hospital B is to indicate that [two] three different types of compounders may be used in combination

to prepare prescription admixtures, such as by but one example, the aforementioned AUTOMIX and MICROMIX compounders. Thus, the compounders 12 may be a compounder adapted for transfer of high volume additives and the compounder 14 may be a compounder adapted for low volume additives. Moreover the compounder 16 may be adapted to transfer both high volume and low volume amounts of ingredients.

The paragraph beginning on page 12, line 19 has been changed as follows:

In an embodiment when high accuracy is desired such as when low volume additives are being added to a PN the fluids from the containers 30 is transferred through a separate individual fluid conduit 32 to a single intermediate container or funnel 34 that is suspended from a load cell assembly 36. The load cell assembly 36 weighs the total weight of the funnel 34 to develop an output signal, which is indicative of the amount of fluid in the funnel [36] <u>34</u> at any given time. The funnel 34 is closed and is connected to a pressure conduit 38 that is connected to a pressure means and occlusion means such as a valve 40 by example. The pressure means is preferably a single peristaltic pump which can selectively create positive and negative pressures in the funnel 34 to control the direction and flow of fluid into and out of the funnel 34. The funnel 34 also is connected to an outlet conduit 42 that extends to a second occlusion means 44 that is interposed

between the funnel 34 and the final bag or container 46. By selectively operating the occlusion means 40 and 44, and the pressure means, fluid can be drawn into the funnel and transferred out of it. These same portions of the machine can also control the direction of flow, so that fluid can be transferred into the final bag 46 and can be removed from the final bag for the purpose of rinsing the funnel 34.

The paragraph beginning on page 13, line 25 has been changed as follows:

Referring to Fig. 3 a further embodiment of a compounder 50 is represented which is particularly suited for transferring large volume additives. The compounder 50 includes a number of individual pumping stations 52 which cooperate with a disposable transfer set 54 to pump fluids from individual source containers 56 to a final container 58. A detailed operation of an example of a compounder adapted to transfer [low] large volume components, at least as of approximately 1999 is described in US Patent Nos. 4,712,590 and 5,927,349 which is assigned to the same assignee as the present invention, and is incorporated by specific reference herein. The current commercial AUTOMIX compounder may embody certain improvements compared to the '485 and '349 patents, but is believed to be similar to that described in the patent.

The paragraph beginning on page 15, line 2 has been changed as follows:

Referring to [figure] Figure [3a] 4a in the preferred embodiment, the pharmacist enters patient identifying data such as a patient ID code into the controller utilizing the keyboard 25 (block 70). The controller 10 then requests and accepts patient specific data (block 72) from a data storage location such as the computer system 28 of the facility and displays such information on the display 23. One type of patient specific data which is preferably utilized by the controller 10 in the preferred embodiment is the patient type such as premature, neonatal, pediatric or adult, etc. In an alternate embodiment, the provider enters the patient specific data directly into the controller 10 or a storage location therein.

The paragraph beginning on page 17, line 5 has been changed as follows:

When an alarm is displayed[. Even] , even though the concentration is outside the range, the concentration may still, in the medical judgement of a provider, be desired. The controller 10 may then in certain predetermined instances allow the provider to override the alarm (block 82). The controller 10 will allow an override upon the occurrence of one or a combination of certain factors. One factor is whether the provider entering the prescription has the clearance to override the particular alarm. [An

each] Each alarm may require a different level of clearance before the override is accepted. Some alarms may not be overridden.

The paragraph beginning on page 17, line 20 has been changed as follows;

In addition to establishing the clearance of the provider, to verify that the provider is recognizing and appreciating the error message and for record keeping purposes[. The] , the controller 10 may require that the rationale for the override be entered into a note screen displayed on the display 23. For certain alarm situations, the controller 10 does not allow any overrides even with a rationale (block 86).

The paragraph beginning on page 18 line 17 has been changed as follows:

The process preferably involves a first screening step of comparing all PN additives to limits set by the controller 10 which may include the steps of setting ranges of preferred concentration limits as described above.

The paragraph beginning on page 18, line 21 has been changed as follows:

A second step involves comparing the final concentration of amino acids, dextrose and lipid based components to the database of tested admixtures. Amino acid comparisons are brand specific. Databases of admixtures have been compiled through the testing of admixtures and also by utilizing published literature. The admixture database preferably comprises concentrations for both stable and unstable admixtures with a notation of the study conditions such as time and temperature. [Preferable] Preferably the database includes admixtures having identified source components such as by example, brand named amino acids.

The paragraph beginning on page 20, line 7 has been changed as follows:

With regard to calcium phosphate solubility screening, the solubility of calcium salts and phosphate salts in the same solution is dependent on many variables including, but [unlimited] not limited to concentration, temperature, salt form, order of mixing, pH, amino acids concentration, other additives and time. It has been the practice in the prior art for the pharmacist to compare the final concentration of both the calcium salt and phosphate salt to a solubility curve that is specific to a given amino acids brand and final concentration.

The paragraph beginning on page 20, line 15 has been changed as follows:

In the present invention, the calcium phosphate solubility screening in a complex compounding process is achieved by the controller 10 comparing the final concentration of both the calcium salt and phosphate salt to a matrix of known compatibility. The matrix may be input into a storage location by the Pharmacist or previously input into the database. The present invention uses the matrix to sort compatibility by the amino acids brand and final concentration. For example, a calcium phosphate solubility matrix for a specific amino acids brand may have compatible concentrations of calcium salts and phosphate salts for a 1%, 2% and 4% final amino acid concentration. The present invention determines the limits of solubility that have been exceeded and will generate a warning to the pharmacist if it has.

The paragraph beginning on page 20, line 26 has been changed as follows:

In a further embodiment, the controller 10 may generate and display on the display 25 a graph of a shape representing the calcium phosphate solubility for [that] which a particular amino acid and may also present a designation of the prescribed

admixture relative to the solubility shape to assist the pharmacist in achieving a prescription which is compatible.

The paragraph beginning on page 21, line 5 has been changed as follows:

However, in addition to [the] determining whether the prescription present in the final bag is compatible, compatibility during the compounding process must be evaluated. For example, the compatibilities of a solution with a second solution at the time of contact must be evaluated. The second fluid may be found in a common conduit, intermediate mixing chamber or final bag. To overcome this potential problem the pharmacist may adopt gross rules for the compounding process. For example it is common practice that all diluent volumes are added to the final bag first so that all additives which are present in the final bag are diluted as much as possible at the time of the addition of an additional ingredient to the final bag. However, such a practice reduces the ability to rinse from such a diluent during the compounding process.

The Table beginning on page 22, line 16 has been changed as follows:

TABLE 1
Group Compatibility

Group	Compatible	Incompatible
1	1, 2, 3, 6	4, 5, 7
2	1, 2, 3, 4, 6, 7	5
3	1, 2, 3, 4, 6[,]	5, 7
4	2, 3, 4, 6	1, 5, 7
5	5, 6	1, 2, 3, 4, [5,] 7
6	1, 2, 3, 4, 5, 6, 7	-
7	2, 6, 7	1, 3, 4, 5

The paragraph beginning on page 24, line 12 has been changed as follows:

In this regard and reiterating what was stated above, while seven separate groups are contained in Table 1, it is expected that additional groups will be defined, which may be based on more sophisticated knowledge and testing. The precise number of groups will eventually be a function of the sophistication of compatibility knowledge vis-a-vis [the all] all the other components that are used, and it is contemplated that a significantly larger number of groups will be defined.

The paragraph beginning on page 25, line 2 has been changed as follows:

In a further embodiment of the present invention a mixing strategy or method which recognizes the possibility of [liquid] lipid hazing and utilizing preferably minimizing rinses from the final bag is shown in FIGS. 4b-4h, which illustrates the preferred embodiment of a method of defining the operation of at least one compounder to provide a nutritional formula admixture. The start (block 100) of the method or process is shown in FIG. 4b and occurs after prescriptions have been entered into the controller computer.

The paragraph beginning on page 25, line 16 has been changed as follows:

In this regard, and as previously mentioned, a hospital, other healthcare facility or pharmacy may have only a high-flow module compounder 12 (FIG. 1) which is adapted to transfer high volume fluids at a relatively high flow rate. However, in the event that the facility also has a low-flow module compounder [12] 14, then it can transfer solutions at a low flow rate, which generally enables very small volumes or amounts of a component to be added to a bag. Therefore, in instances where particularly adopted high volume and low volume compounders are utilized, the controller decides compounding strategy (block [2] 102) determines which strategy to employ. The

program is adapted to control either a high flow rate (block 104) which would control a high-flow module compounder for example, a low flow rate (block 106) which would control a Low-flow module compounder, for example, or a high and low flow rate (block 108) which would result in both machines being used or for a single compounder 16 suitable for both high volume and low volume transfers, for example.

The paragraph beginning on page 26, line 5 has been changed as follows:

Referring initially to the high flow only, the controller performs initial compounder calculations for high flow only compounder set up (block 104) which comprises several calculations that the program will execute for each large volume component that will be part of the final bag. This includes the calculation based on specific gravity to convert volume measure to weight measure, if the transfer is carried out by utilizing the weight of a component that is transferred rather than volume that is transferred. In this regard, a prescription may be written using measurements that are input by grams or milliliters or a percentage of the final solution and the software may be required to convert the measurements to weight, if the compounders transfers in dependence on the sensed weight of the transferred component. For example, the high-

flow module [14] 12 and low-flow module compounders [12] 14 compound utilizing the weight or change of weight of an intermediate or final container.

The paragraph beginning on page 26, line 26 has been changed as follows:

This involves the sorting of all the additives into compatibility groups [such as compatibility groups] and this is done by grouping common compatibility components as shown in the Table 1 above. If lipids are transferred first in the final bag, a determination of the number of compatibility meta-groups is made and the number of rinses N that will be required (block 114) and then the program specifies a sequence of large volume transfers with lipids first. Once the sequence is determined, then line 118 extends to FIG. 4d where the instructions for operating the compounder are transferred to the compounder (block 120).

The paragraph beginning on page 27, line 23 has been changed as follows:

If the compounder 14 has separate conduits to the final bag for each of the source solution, the controller 10 [set] sets the order of pumping to insure that [the] as fluid is added to the final bag, the primary determination of the order of pumping is the compatibility of the fluid entering the bag with the fluid present in the bag.

The paragraph beginning on page 28, line 2 has been changed as follows:

Returning to FIG. 4c, if the lipids are not first in the final bag, the number of compatibility groups is also determined, as is the number of rinses required (block 122) and the sequence of transfers and rinses with lipids last [is] determined using one or more of the compounding methods is executed and the final step shown by line 126 that extends to FIG. 4d results in the transfer instructions being sent to the compounder (block 120).

The paragraph beginning on page 30, line 7 has been changed as follows:

The determination is made as to whether lipids are included in the final bag (block 152). If lipids are required, the determination is made whether lipids are to be transferred first, last or otherwise optimized (block 154). Whether lipids are required to be first, last or optimized is a user preference that is programmed in the sense that the user defines this once and it is thereafter not prescription dependent. Optimize usually always means that lipids would be placed first. Thus, the criteria for compounding that is established by the user initially will determine the path of steps taken. If they are first or optimized, then line 156 extends to FIG. 4d and FIG. [4c] <u>4e</u> to a step that will be described later. If lipids are not included in the final bag, then line 158 extends to FIGS.

4d and 4e for steps that will also be described later. If lipids are required to be last, then line 160 extends to FIG. 4d and the determination is made whether the prescription is stable without the lipid volume (block 162).

The paragraph beginning on page 30, line 21 has been changed as follows:

If the prescription is not stable without the lipid volume, the program alerts the user that the prescription cannot be compounded if lipids are last and that a pharmacist check may be required (block 164). The program then determines whether lipids can be transferred into the final bag first (block 166), which if not, results in the compound not being prepared (block 168). If the lipids can be transferred first, then line 170 extends to FIG. [3d] 4e wherein the number of rinses including the volume of lipids and lipids will be transferred to the final bag first (block 172).

The paragraph beginning on page 31, line 3 has been changed as follows:

Returning to block 162, if the prescription is stable without including the lipid volume, then the program calculates all solubilities without including the volume of lipids and the lipids will be transferred to the final bag last (block 174) (FIG. 4d). The calculation of solubilities not including the volume of lipids (block 174) is done to

calculate the calcium phosphate solubility based on possibly less volume than what was included in the original screening. Therefore, for example, if there were 50 milliliters of lipids in a 200 milliliter total volume PN, then the phosphate calcium solubility evaluation would be done on 150 milliliters.